



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/749,699 | 12/30/2003 | Terry B. Strom | 13985-057002 | 9466 |
| 26161 7590 06/20/2008 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022 | | | | |
| EXAMINER | | | | |
| HAMUD, FOZIA M | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1647 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 06/20/2008 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/749,699

Applicant(s)

STROM ET AL.

Examiner

FOZIA M. HAMUD

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,35,36,42-45 and 47-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,35,36,43-45,47,48,50 and 51 is/are rejected.
- 7) ☒ Claim(s) 42 and 49 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 12/12/2008.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Detailed Action

Request For Continued Examination:

1a. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 March 2008 has been entered.

Status of Claims:

1b. Claims 2-34, 37-42, 46 and 49 are cancelled. Thus, claims 1, 35-36, 42-45, 47-51 are under consideration.

Specification:

1c. The amendment to the specification updating the status of parent applications and correctly labeling figures 1 and 2 is acknowledged. Figure 1 represents mutant IL-15, having aspartate at positions 149 and 156, while figure 2 represents wild type IL-15. The two figures are now correctly labeled. No new matter has been added.

Information Disclosure Statement:

2. The IDS submitted on December 12, 2003 have all been considered on April 16 2006. However, the U.S. patents, foreign patents, cited on sheet one of four of said IDS, were inadvertently not initialed. The references cited on page one of the IDS of 12/12/2003 have now been initialed.

Response to Applicant's Argument:

3. The following rejections are withdrawn in light of Applicants' arguments:
- I. All of the rejections of cancelled claims are moot.
 - II. The rejection of claims 1, 35-36 and 42-45 made under 35 U.S.C. 112, first paragraph, for not enabling the full scope of the claims is withdrawn, because the claims now encompass an IL-15 mutant that has specific mutations.
 - III. The rejection of claims 1 and 42-45 made under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is withdrawn, because the claims now encompass an IL-15 mutant that has specific mutations.
 - IV. The rejection of claims 1 and 45 made under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, by introducing new matter is withdrawn. Applicants correctly point out that the rejected limitation, "binds IL-15R but fails to fully activate signal transduction through the IL-15R.", is disclosed on page 15, lines 8-9 of the specification. Thus, said limitation which is now deleted from the claims, is not new matter.
 - V. The rejection of claims 1, 35-36 and 42-45 made under 35 U.S.C. 112, second paragraph, for reciting "...but fails to fully activate signal transduction through the IL-15R...", is withdrawn, because said limitation is deleted.
 - VI. The rejection of claim 44, made under 35 U.S.C. 112, second paragraph, for reciting "...is a target-cell deleting FC regions ...", is withdrawn, because Applicants' argument that the structure of target -depleting Fc, is fully described and defined in the specification has been found persuasive.

Maintenance of Previous Rejections:

Claim rejections-35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The rejection of claims 1, 35-36, 43-45, 47-48 and 50-51 made under 35 U.S.C. 103(a) as being unpatentable Kim et al (The Journal of Immunology, 1998. Vol. 160, pages 5742-5748) in view of Strom et al (Transplantation Proceedings, 1995. Vol. 27, No.5, pages 18-20), is maintained, because the combined teachings of Kim et al and Strom et al render the claimed composition obvious.

Applicants argue that the fact that two therapeutic agents were reported to have immunosuppressive activity is no indication that they would necessarily work together, or that they would work better than each agent alone. Applicants further submit that IL-2 and IL-15 have overlapping activities because they bind to the same receptors, thus it does not flow logically that a combination of agents having an overlapping receptor

specificity would be useful and have redundant functions. Applicants contend that Kim used knowledge of IL-2 to move from an IL-2-related treatment to an IL-15-related treatment, but never suggested that the two agents should be combined, which indicates that an IL-15R targeting agent is interchangeable with an IL-2R targeting agent, thus there is no motivation to use two such agents together. Applicants disagree that In re Kerkhoven is relevant to considerations of obviousness in this case.

Applicants submit that in re Kerkhoven is concerned to combinations of detergents, prior art describing the properties of various detergents may be suggestive, where it is common to mix them based on shared properties. However, Applicants argue that this principle is not applicable to all technical fields. Applicants contend that there is no indication in the cited art that it is common to create mixtures of therapeutic polypeptides simply because they share a biological function and that the claimed compositions arise from the inventors' discovery of novel ways to inhibit the immune response. Applicants argue that the ability of IL-2/Fc to promote activation induced cell death is not suggested or recognized in the cited references, not to mention its use in combination with an agent that promotes passive cell death. In addition, the inventors have discovered that the claimed combinations have unexpected potency. The specification describes an experiment in which mice received transplants of allogeneic skin grafts. Administration of a composition including both mutant IL-15/Fc and IL-2/Fc more than doubled the mean survival time of functioning grafts as compared to graft survival in animals administered a composition including only one of the agents, thus, a

Art Unit: 1647

combination of agents having these features provides superior immunosuppressive effects.

These arguments have been fully considered, but are not deemed persuasive. The combined teachings of the cited references render the claimed invention obvious. Kim et al teach an IL-15 mutant/Fcγ2a antagonist with immunosuppressive activity and demonstrate that targeting of IL-15R can abrogate an in vivo-Th1 response and the authors suggest that this fusion protein can be used in diseases such as organ transplantation or inflammatory diseases. Strom et al teach a fusion protein which comprises IL-2 fused to Fc region of immunoglobulin and teach that said chimera is cytolytic and retains in vivo efficacy as an immunosuppressive agent. Thus, the combined references disclose that each agent has immunosuppressive activity and the skilled artisan would expect that the combined agents would have significantly better results. With respect to Applicants' argument that IL-2 and IL-15 have overlapping activities and have redundant functions, the two peptides bind the same beta and gamma chains but different alpha chains so it would be expected saturation binding at the beta and gamma chains and coverage of each different alpha chain. Thus, it would be expected better binding overall by combining the two agents. Contrary to Applicants' argument, in re Kerkhoven is relevant to considerations of obviousness in this case, because the courts have held:

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Although in re Kerkhoven is concerned claims to combinations of detergents, it is relevant in the instant case, because the prior art teaches that each agent of the claimed composition has an immunosuppressive activity and the skilled artisan would expect that combining them would have higher immunosuppressive activity.

With respect to Applicants' argument that the ability of IL-2/Fc to promote activation induced cell death is not suggested or recognized in the cited references, Applicants are arguing limitations not recited in the instant claims. Finally, with respect to Applicants' argument pertaining to unexpected results, although it is persuasive that a combination of lytic IL-2/Fc, mutIL-15/Fc and rapamycin proved effective in preventing graft rejection and was unexpectedly more effective than either agent alone, (see figures 11 and 12), the instant claims are not drawn to a composition comprising lytic IL-2/Fc, mutIL-15/Fc and rapamycin. The instant specification has not demonstrated that a composition comprising lytic IL-2/Fc, mutIL-15/Fc would also have the same unexpected results.

Claim Objections:

- 5a. Claims 42 and 49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- 5b. The attorney was contacted in an attempt to amend the claims in condition for allowance, however, the attempt was not successful.

Conclusion:

6. No claim is allowed.

Art Unit: 1647

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FOZIA M. HAMUD whose telephone number is (571)272-0884. The examiner can normally be reached on Monday-Friday: 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
29 May 2008

/Bridget E Bunner/
Primary Examiner, Art Unit 1647